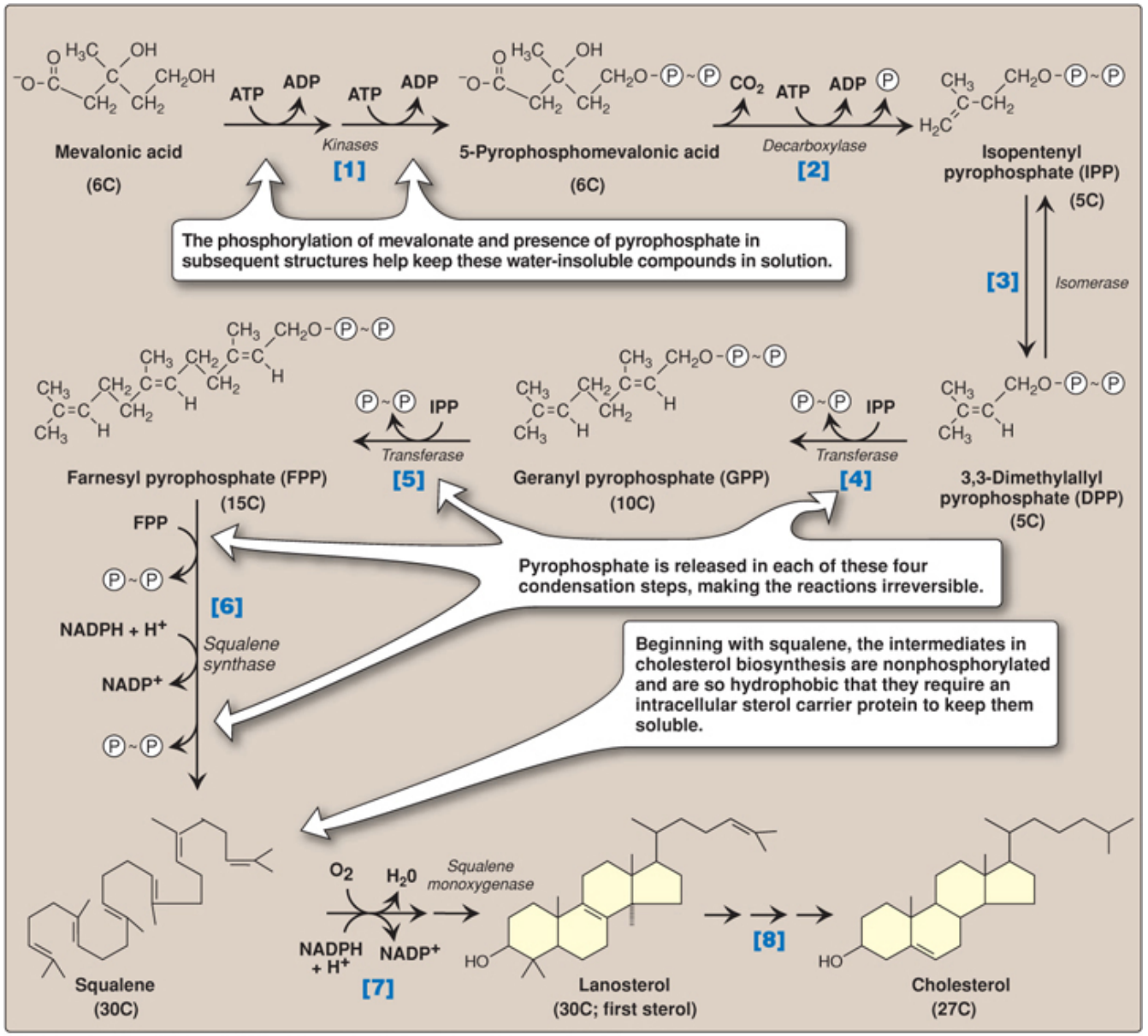
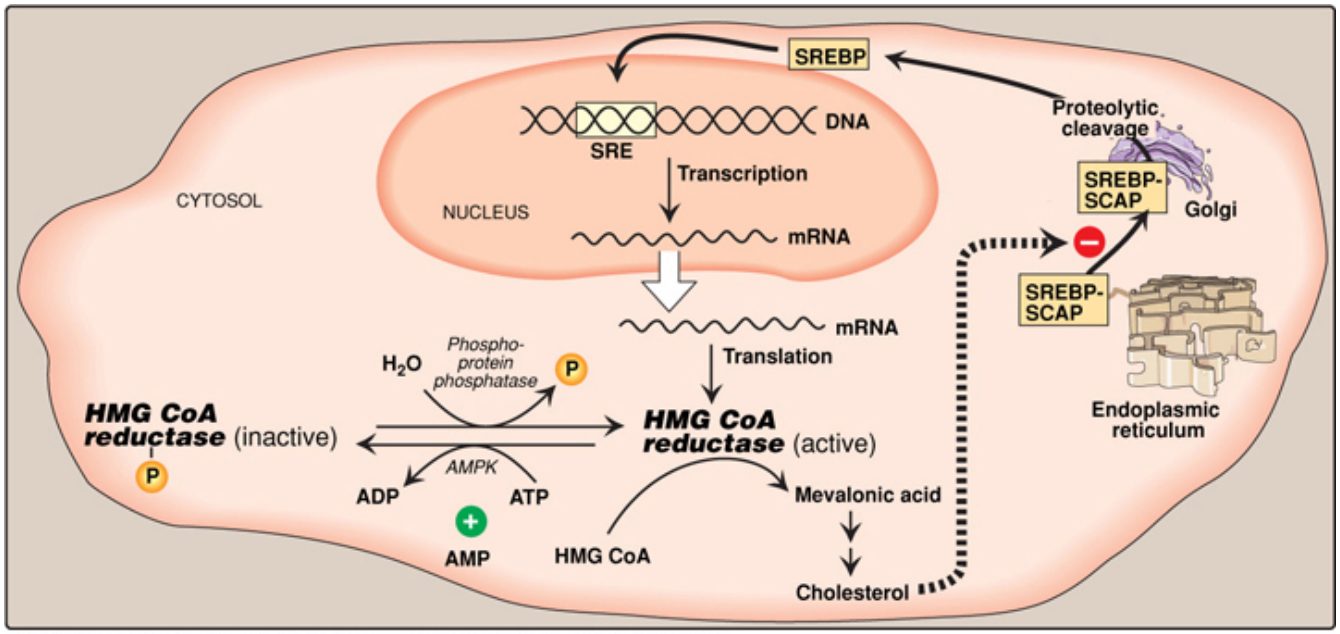
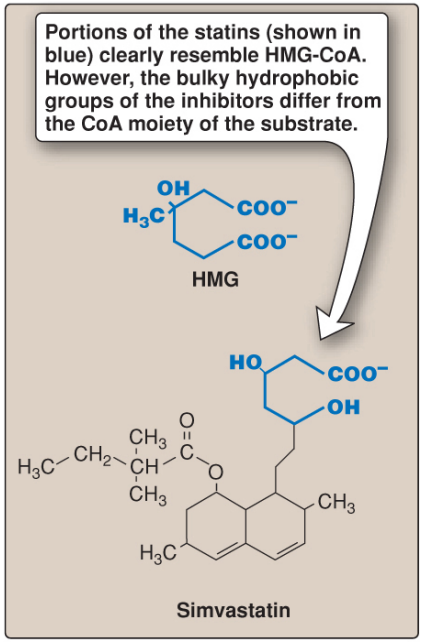




Regulation of HMG CoA reductase

1. regulation of gene expression by SREBP
2. phosphorylation state
3. regulation by hormones (insulin, glucagon)
4. inhibition by statin drugs



Regulation of HMG CoA reductase

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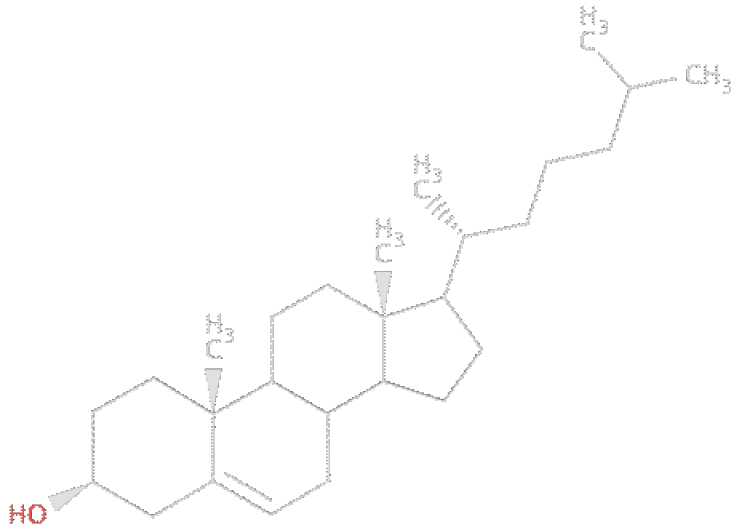
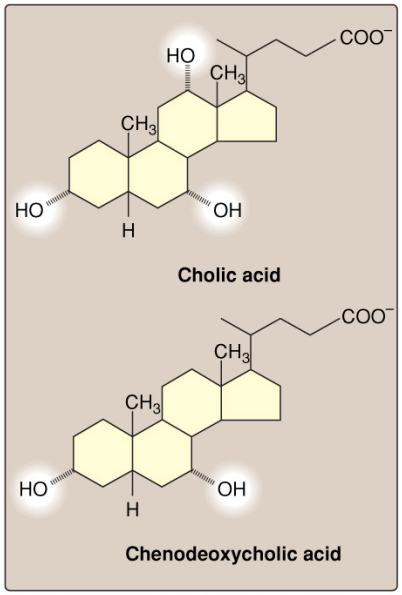
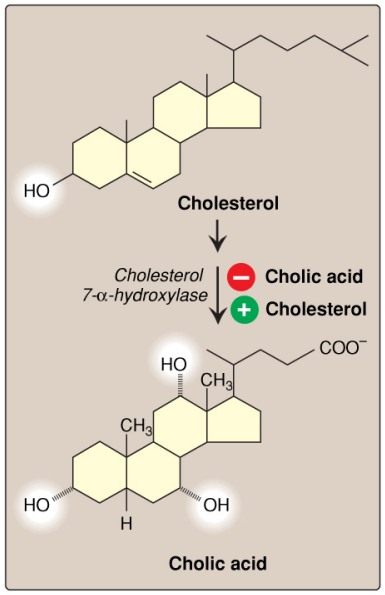
Degradation of Cholesterol

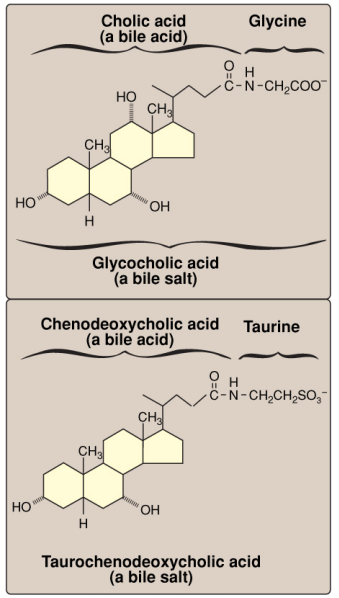


- The ring structure of cholesterol cannot be metabolized to CO_2 and H_2O in humans.
- The sterol ring nucleus is eliminated from the body by conversion to bile acids and bile salts.

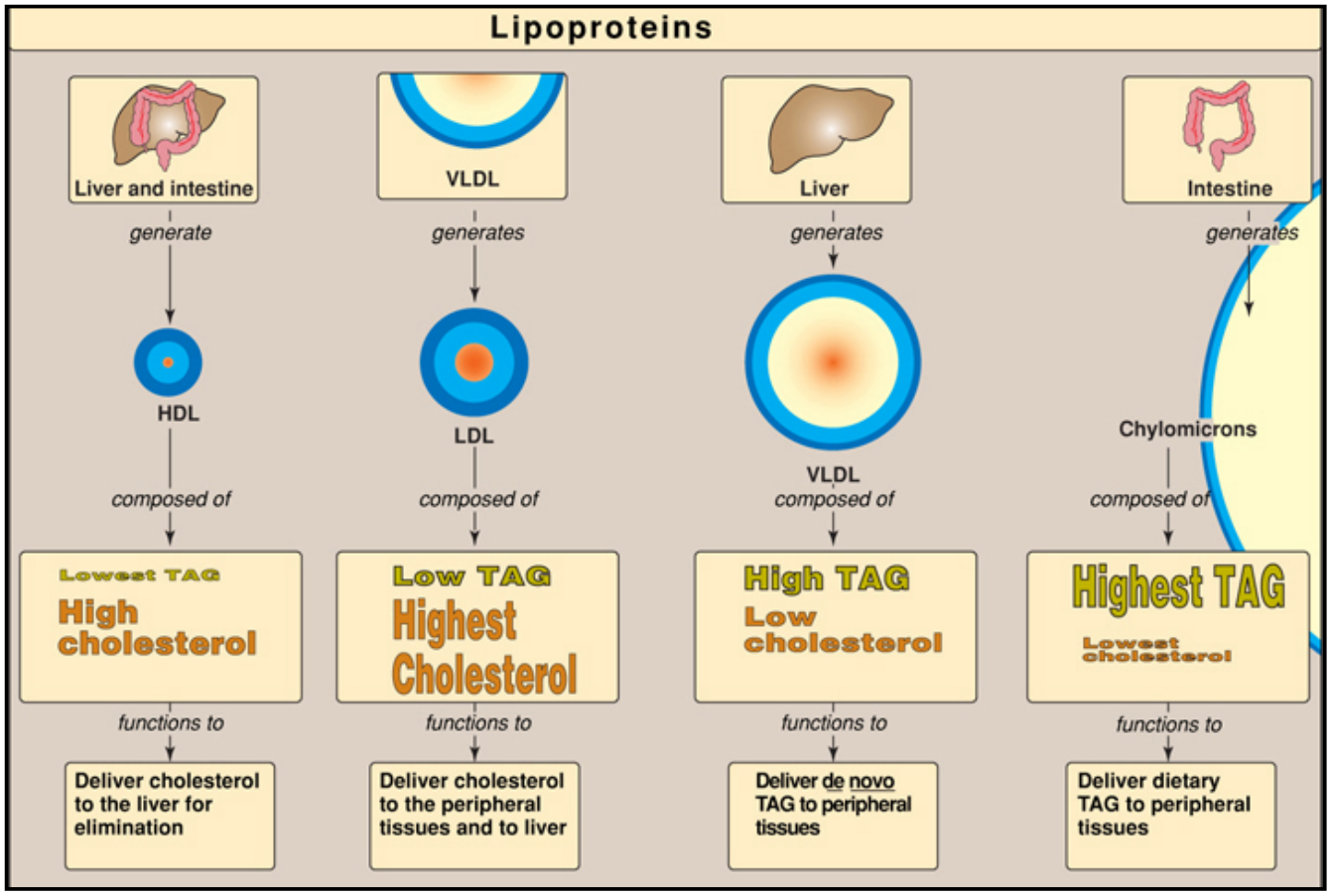
Degradation of Cholesterol



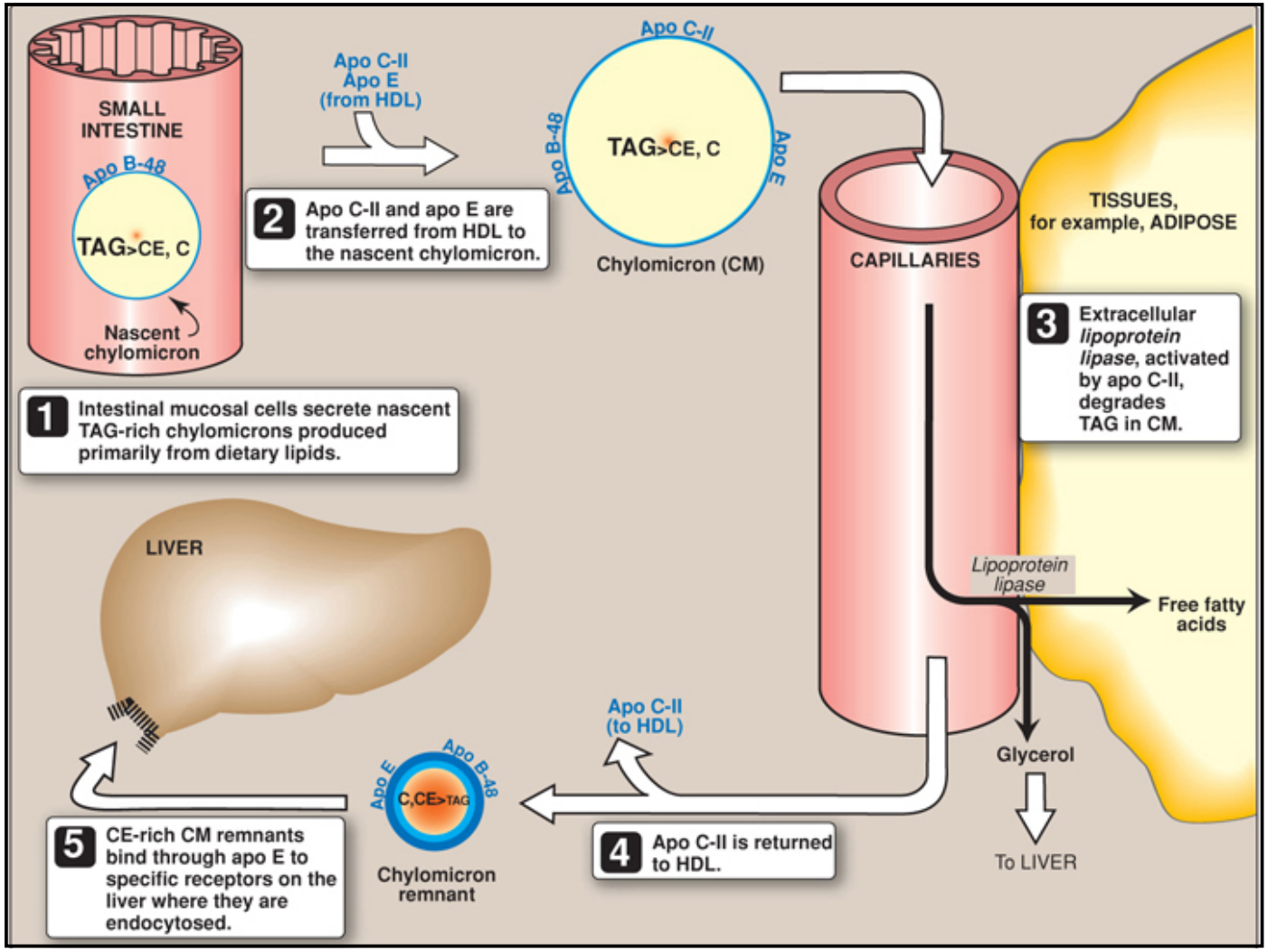




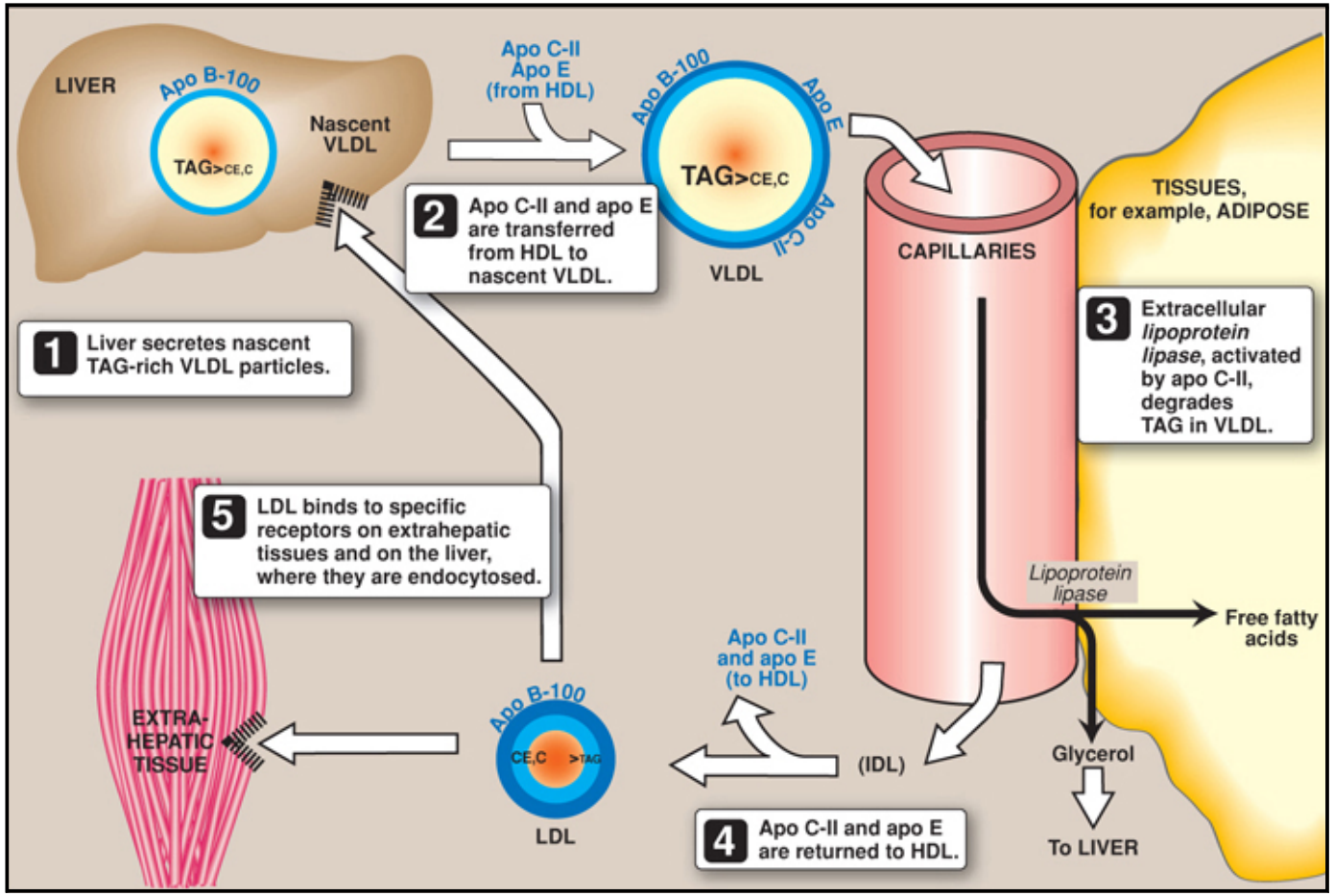
- The theme is for cholesterol to be converted to a relatively soluble amphipathic molecule.
- As a bonus, these molecules are used as emulsifying agents during digestion.



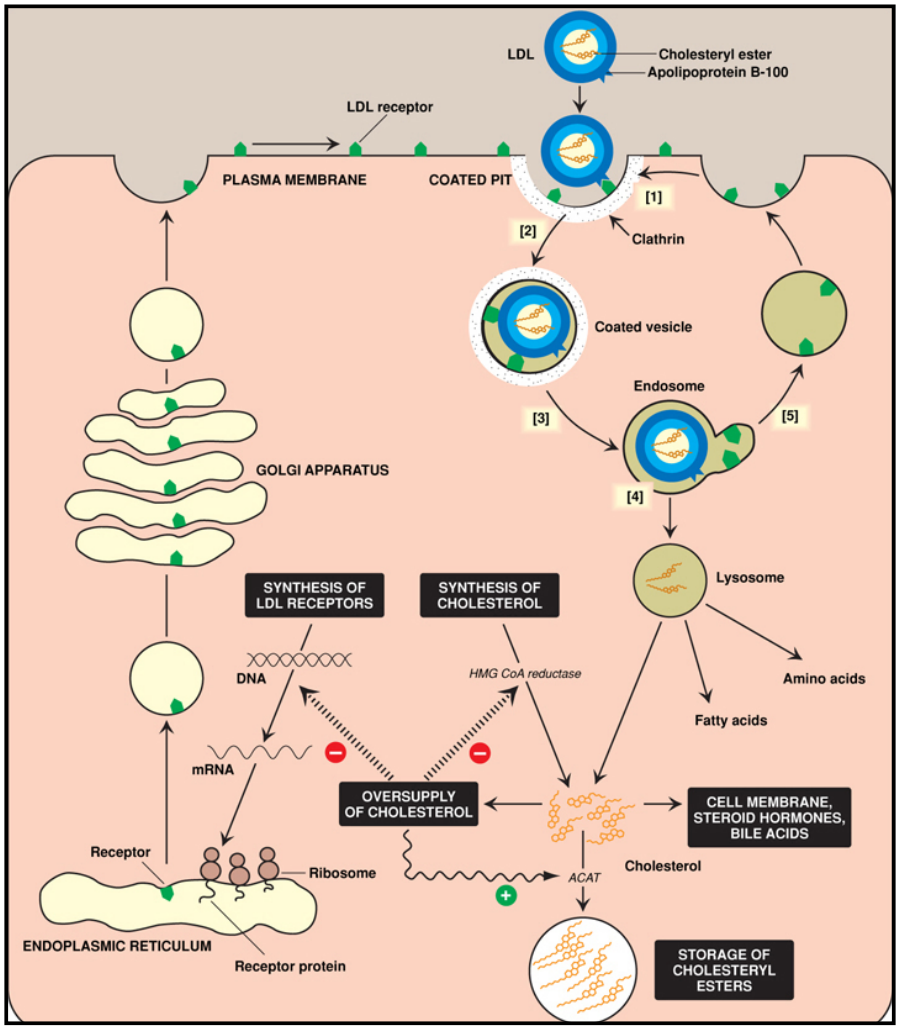
Delivery of fatty acids and cholesterol via plasma lipoproteins



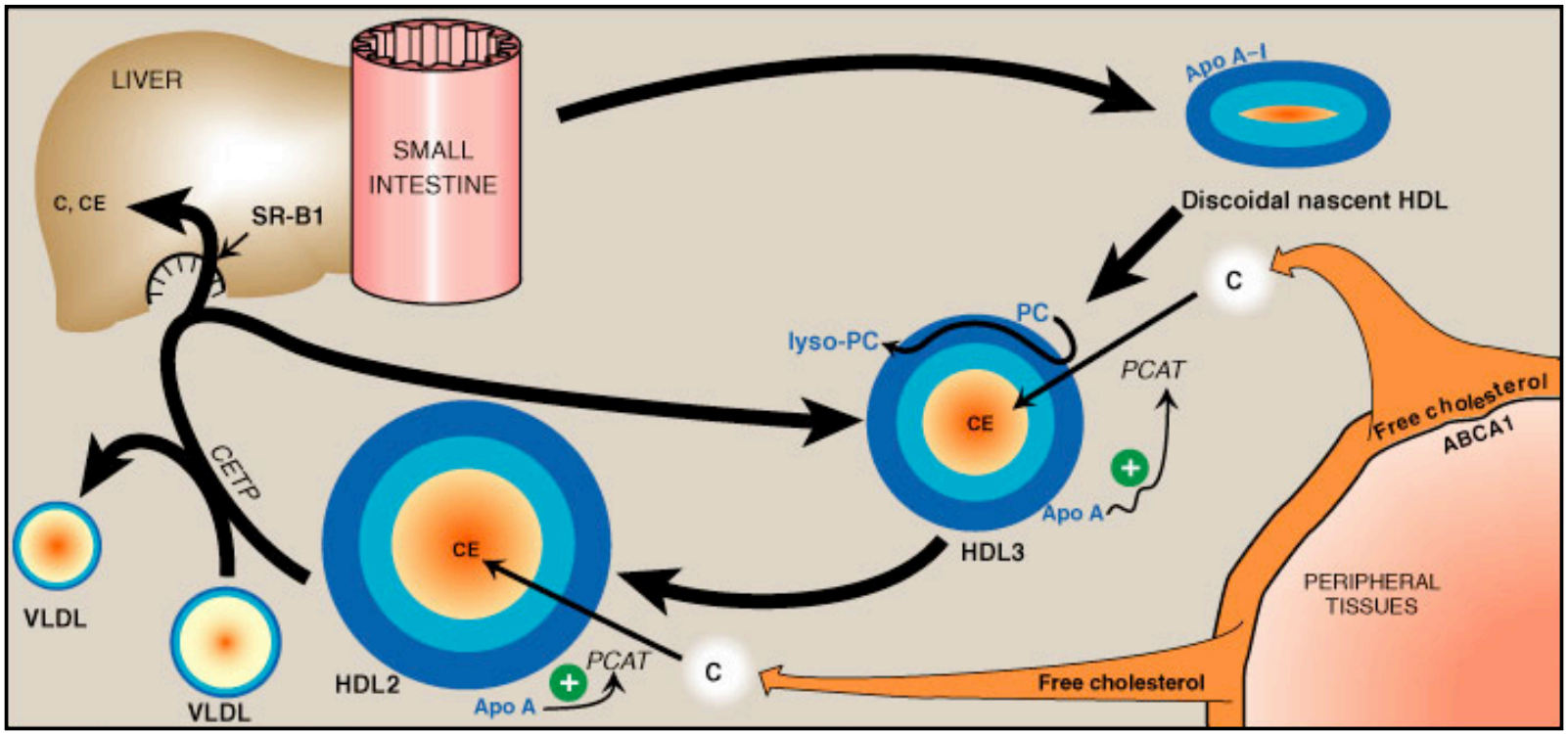
Chylomicrons deliver TAG's and return to the liver



VLDL (pre-LDL) deliver some TAG's and bulk cholesterol



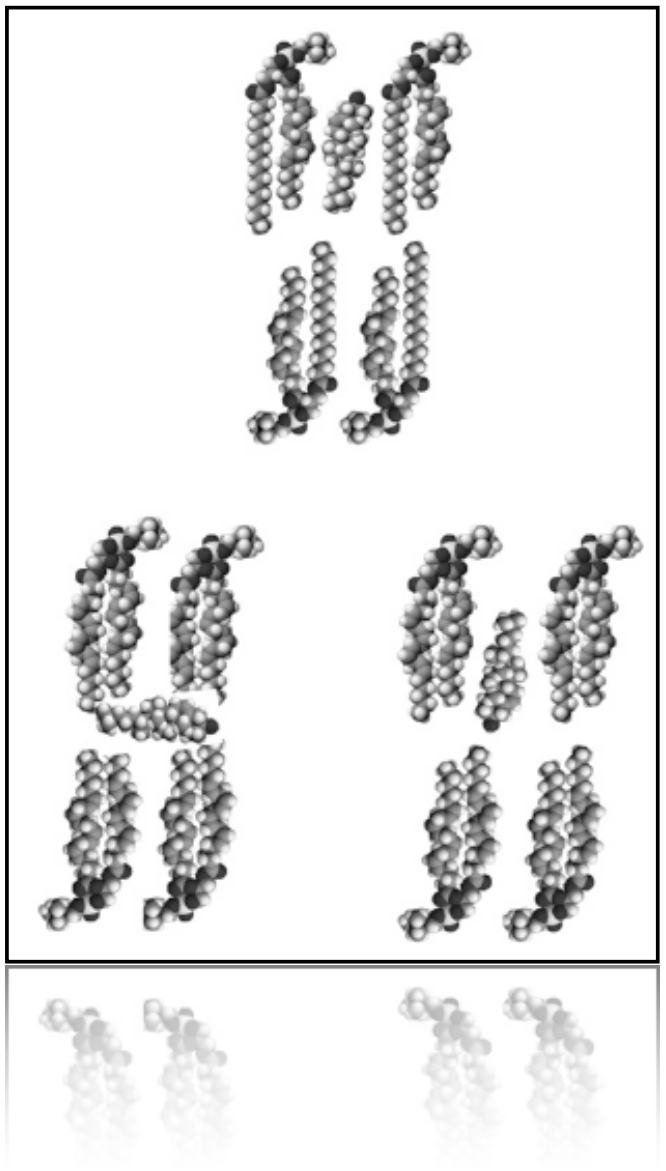
LDL delivers cholesterol directly to the interior of cells



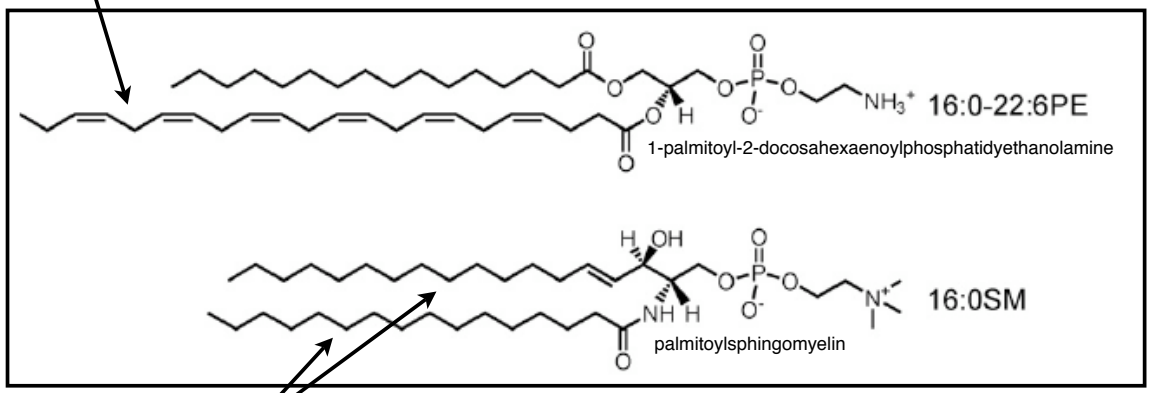
HDL are secreted ‘empty’ and scavenge cholesterol

In cells, cholesterol distributes into membranes

- cholesterol has limited flexibility and is a fairly rigid structure.
- stiffens the membrane and makes it less permeable
- it can interact with and affect the structure of integral membrane proteins



docosahexaenoate (DHA)



palmitate

lipid rafts form due to spontaneous segregation between DHA and SL containing membrane lipids

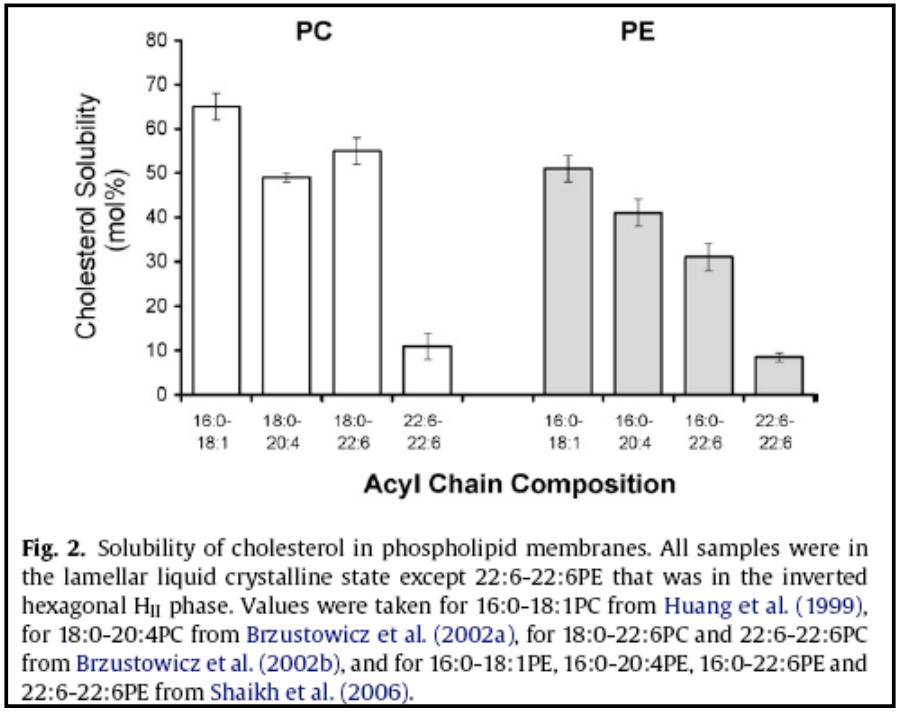


Fig. 2. Solubility of cholesterol in phospholipid membranes. All samples were in the lamellar liquid crystalline state except 22:6-22:6PE that was in the inverted hexagonal H_{II} phase. Values were taken for 16:0-18:1PC from Huang et al. (1999), for 18:0-20:4PC from Brzustowicz et al. (2002a), for 18:0-22:6PC and 22:6-22:6PC from Brzustowicz et al. (2002b), and for 16:0-18:1PE, 16:0-20:4PE, 16:0-22:6PE and 22:6-22:6PE from Shaikh et al. (2006).

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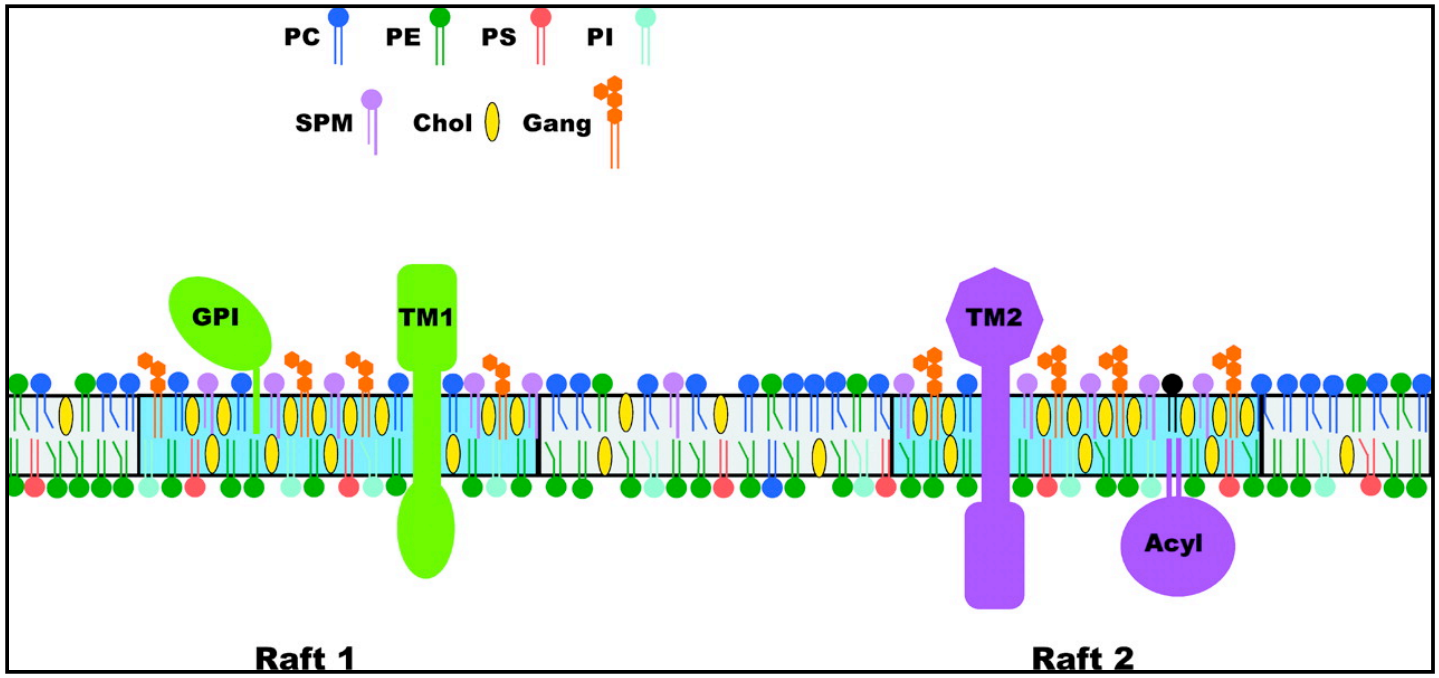
Cholesterol is less soluble in (artificial) membranes high in unsaturated acyl chains


PC
PE
PS
PI
SPM
Chol
Gang
GPI
TM1
TM2
Acyl
Raft 1
Raft 2

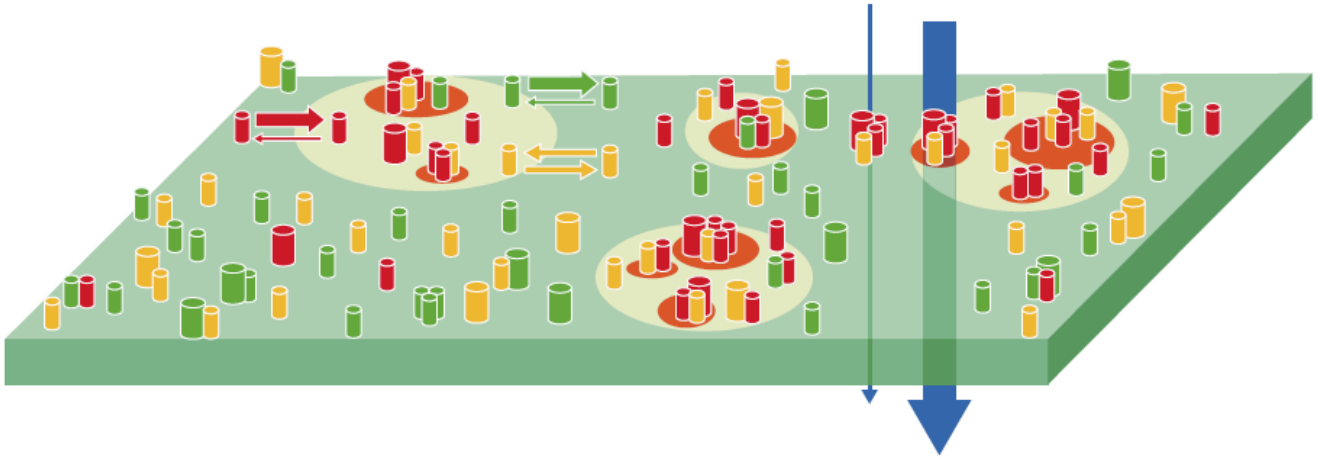


Fig 2 | Formation of specific molecular assemblies promoted by dynamic nanodomain partitioning for efficient receptor signalling. By promoting temporary lateral confinement, raft nanodomains might contribute to the formation of molecular assemblies, especially those based on weak protein–protein or protein–lipid interactions that might otherwise be insufficient for such a formation in a disordered membrane environment. In this way, nanodomains could have an important role in organizing specific components of the receptor signal machinery for speedy and efficient triggering on ligand engagement. The thickness of the vertical arrows indicates the efficiency of signal triggering.

He and Marguet, EMBO *reports* VOL 9 | NO 6 | 2008

Lipid rafts are thought to promote molecular assemblies and to drive conformational changes in membrane proteins